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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,416	04/13/2000	MICHEL REVEL	REVEL=15	5069

1444 7590 10/02/2002

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EXAMINER

BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 10/02/2002 15

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/462,416

Applicant(s)

Rehovot et al

Examiner

Nirmal S. Basi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jul 10, 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2-7, 9-11, 16-26, 33, 37, and 38 is/are pending in the application.
- 4a) Of the above, claim(s) 16-26 and 37 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-7, 9-11, 33, and 38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

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### **DETAILED ACTION**

1. Amendments filed 7/10/02 (paper number 14) has been entered.

2. Applicant has again traversed the Restriction Requirement stating that, "The claims have now been amended in a manner so as to clearly and definitely avoid anticipation by Fischer" and

5 "the claims now ultimately depend from claim 38, they all share the same common technical feature". Applicants arguments have been fully considered but not found persuasive. As indicated in paper number 10 and 13 the special technical feature of Group I was found in the prior art and therefore unity of invention was lacking for the claimed inventions. The claims were restricted into VI groups. Applicant has deleted claim 1 and amended claim 2 to overcome  
10 the anticipation of the claims by Fischer. The lack of unity was made on the claims present in the Application prior to mailing of paper number 10 (Restriction Requirement). Since applicant has received an action on the merits for the originally presented invention (Group I), which lacked unity of invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 16-26, and 37 are withdrawn  
15 from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

### **Claim Rejection, 35 U.S.C. 112**

3. Amended claims 2-7, 9-11, 33 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject  
20 matter which applicant regards as the invention.

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Claim 38 is indefinite because it is not clear what is the amino acid sequence of the Ig-like domain and receptor pre-membrane domain of the sIL-6R so as to allow the metes and bounds of the claim to be determined. The Ig-like domain and receptor pre-membrane domain of the sIL-6R have not been defined so as to allow their amino acid sequence to be determined.

Claim 38 is indefinite because it is not clear what is the naturally occurring form of sIL-6R or IL-6 so as to allow metes and bounds of the claims to be determined. The preamble states "A chimeric glycosylated soluble interleukin-6 receptor (sIL-6R)-interleukin-6 (IL-6) polypeptide (sIL-6R, comprising" and subsection (a) states "an amino acid sequence which is a fusion product of the naturally occurring form of sIL-6R" and "the naturally occurring form of IL-6. Therefore for the metes and bounds of the claim to be determined the glycosylation pattern of the naturally occurring of sIL-6R or IL-6 must be known. The glycosylation pattern of the naturally occurring of sIL-6R or IL-6 is not defined.

Claims 3 is indefinite because it is not clear when linker is very short so as to be about 3 amino acids residues. Specifically when is a linker considered short or very short as compared to when it considered not short vert short so as to be about 3 amino acid residues. The "term very short, non-immunogenic linker of about 3 amino acid residues" does not allow the metes and bounds of the claim cannot be determined.

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Claims 2, 4-7, 9-11 and 33 rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

**Claim Rejection, 35 U.S.C. 112**

5        4.        Amended 2-7, 9-11, 33 and 38 are rejected under 35 U.S.C. 112, first paragraph, because  
the specification, while being enabling for the chimeric sIL-6R/IL-6 chimera disclosed in SEQ ID  
NO:7, chimeric sIL-6R/IL-6 chimera disclosed in SEQ ID NO:7 in which the 13 amino acid  
peptide linker of SEQ ID NO:1 is substituted for the Glu-Phe-Met of residues 357-359 of SEQ  
ID NO:7, analog of chimeric sIL-6R/IL-6 which differ from the sequence disclosed in claim 38  
10        (a) by no more than 30 changes in the amino acid sequence, such change being a substitution,  
deletion, addition or insertion of a single amino acid, which is capable of triggering the  
dimerization of gp130 in human cells does not reasonably provide enablement for other chimeric  
constructs. The, specification does not enable any person skilled in the art to which it pertains, or  
with which it is most nearly connected, to make and use the invention commensurate in scope  
15        with these claims.

While the person of ordinary skill in the art would, in light of the specification be able to  
isolate make the “enabling” sIL-6R/IL-6 chimeric constructs disclosed above, the specification  
nor prior art disclose which amino acid are critical for structure and function, and how mutation  
could effect the activity of other the chimeric constructs.    The specification does not disclose  
20        how to use the non-functional chimeric constructs encompassed by the claim. If the peptide

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linker is too short, too long, immunogenic in nature, the chimeric construct may not function to trigger dimerization of gp130 in human cells and the chimeric construct will not be capable of use as a pharmaceutical agent. A given peptide linker may not have the same significance in different peptide sequences, or even in different positions of the same sequence. Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for functional chimeric protein, comprising sIL-6R/IL-6, would prevent the skilled artisan from determining whether any modification or mutation to the construct molecules could be made which retains the desired function of the instant invention, because any random mutation or modification manifested within said protein itself would be predicted to adversely alter its biologically active 3-dimensional conformation, without undue experimentation to determine otherwise. Due to the large quantity of experimentation necessary to make fusion proteins with non immunogenic linker, the lack of direction/guidance presented in the specification regarding what linker are non-immunogenic and function to retain the biological activity of the chimeric constructs claimed, the lack of direction/guidance as to the identification, purification, isolation and characterization of chimeric constructs of naturally occurring glycosylated sIL-6R, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:7, are also encompassed by the claim), and the breadth of the claim which fail to recite specific functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

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**Advisory Information**

5           Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

10           If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

            Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

15           Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi

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20           October 1, 2002

*Michael D. Pak*  
MICHAEL PAK  
PRIMARY EXAMINER